REMARKS

Applicant thanks the examiner for entering the amendments to claims 28 and 29, for considering new claims 32-43 and for considering the references filed in the Information Disclosure Statements. Applicant expressly reserves the right to file divisional applications or to take other such appropriate measures deemed necessary to protect the inventions in the cancelled claims 1-27 and 30-31.

In this Amendment and Response, claims 29, 36, 42 and 43 are being amended. Support for the amendment to claim 29 can be found in the specification at, for example, paragraph [00182] or [00189]. Support for the amendment to claims 36, 42 and 43 can be found in the specification at, for example, paragraph [0068] or [00175]. These amendments do not add new matter.

The Examiner's remarks in the Office Action are addressed below in the order set forth therein.

Objection to the Specification

The Examiner objected to the presence of lines to complete sentences in paragraph [0023]. Applicant respectfully refers to the amendments to the specification filed in the previous response mailed on June 21, 2005. At page 2 of that response, Applicant requested that paragraph [0023] be deleted. Withdrawal of this objection is respectfully requested.

The Examiner also warns against hyperlinks in the specification. Applicant respectfully directs the Examiner's attention to pages 3 to 5 of the amendments made in the paper described above. On those pages, Applicant amended the specification to remove browser executable code. If there is any specific objection to these amendments, Applicant respectfully requests additional guidance in the next communication.

Rejection of Claims Under 35 U.S.C. §112, second paragraph

Paragraph 5. Claims 29, 32 and 37-42 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner treats individual claims separately, so they will be addressed separately below.

Claim 29 (claims 37-39 dependent thereon) was rejected as being indefinite for the recitation of "direct" detection of binding and use of the term "test compound/polypeptide binding." Clarification of the phrases was requested. In response, Applicant is amending this section of claim 29 to recite detection of a complex of the test compound with the polypeptide.

Claim 29 also was rejected, as well as claims 40 (claim 42 dependent thereon) and 41, as being indefinite because of a lack of understanding of the term "93870-mediated signal transduction" and how an assay for such activity indicates whether the test compound has bound to the polypeptide. Applicant

points the Examiner to paragraph [0052] where 93870-mediated signal transduction is disclosed and further explained in paragraphs [0050]-[0054]. As is evident in these paragraphs, binding of a molecule, e.g. a ligand, to 93870 would be detected in an assay for the resulting signal transduction.

Claim 32 was rejected as being indefinite because of a lack of understanding of the term "directly and indirectly labeled." Applicant respectfully directs the Examiner's attention to paragraphs [00199] and [00207], which provide some non-limiting examples of indirect labeling, to provide context of understanding for direct and indirect labeling, such as disclosed in those paragraphs and paragraph [00189].

Claim 41 was rejected as being indefinite because of a lack of understanding of the term "mobilization of a molecule." Applicant respectfully directs the Examiner's attention to paragraph [0052] wherein this term is derived and to paragraphs [0053] and [0054] wherein this term is illustrated in the examples of metabolism, turnover and activities of the recited molecules.

In view of the amendment to claim 29 and the remarks on that claim and the other claims in this section, Applicant respectfully requests withdrawal of the rejections of claims 29, 32 and 37-42.

Rejection of Claims Under 35 U.S.C. §101

Paragraph 6. Claims 28-29 and 32-43 were rejected under 35 U.S.C. §101, because the claimed invention apparently is not supported by either a specific and substantial asserted utility or a well established utility. The Examiner provides several examples to support this rejection, such as the inability to find in the specification disclosure of information such as a) significant structural homology to any known GPCR which could be used to predict its activity or signal transduction pathway, b) the individual regions of SEQ ID NO:2 which form the seven transmembrane regions; c) the catalytic domain of SEQ ID NO:2; d) the G protein that couples to SEQ ID NO:2; e) the natural ligand that binds SEQ ID NO:2; f) specific diseases that are directly related to the GPCR dysfunction; g) the activity regulated by SEQ ID NO:2; h) diseases that can be treated by the candidate compound indentified by binding to SEQ ID NO:2; i) experimental data on the functionality of SEQ ID NO:2; j) the specific activity of the claimed GPCR; and k) the ligands that bind or activate the GPCR. The Examiner notes the disclosure of SEQ ID NO:2 as a GPCR and an involvement in an alleged variety of unrelated disease states, but concludes that the skilled artisan cannot come to the conclusion as to the function of the protein. Applicant respectfully traverses this rejection.

First, for statements a), b) and c) above, Applicant respectfully directs the Examiner's attention to the specification at, for example, paragraphs [0024]-[0044], wherein information regarding the structural characteristics identifying SEQ ID NO:2 as a GPCR, in particular a member of GPCR subfamily I, is disclosed. For example, the structure of SEQ ID NO:2 is dissected to disclose locations of the transmembrane domains and intervening loops and a characteristic subfamily I and GPCR consensus

sequences are identified. The specification also describes results of an alignment with SwissProt P51676, a known mouse GPCR. From these disclosures, a skilled artisan could readily recognize SEQ ID NO:2 as a seven transmembrane receptor and a GPCR of subfamily I. Further, in regard to statements d) and j), paragraph [0052] explains certain well-known features of activities of GPCRs, so the skilled artisan could readily envision cellular responses to the activity of SEQ ID NO:2.

By extension of the Examiner's statement, at page 8, one would reason that a utility to an orphan receptor can be assigned with knowledge of what disease is associated with the claimed receptor or what drugs/ligands effect a specific receptor function. Applicant asserts that the specification does disclose specific diseases in which SEQ ID NO:2 has a role. Applicant respectfully requests entry into the record data confirming such specific diseases. A Declaration by Dr. Timothy Ocain, under 37 C.F.R. § 1.132, verifies data submitted therewith as Exhibit B and explains its use in a decision, in 2002, to include the 93870 GPCR in an Inflammation discovery program at Millennium Pharmaceuticals, Inc.. The data, compiled and presented to Dr. Ocain by Dr. Ethan Grant, provides additional homology information and an approach to deorphaning 93870 as a purinergic receptor. The data also confirm the utility of 93870 GPCR as having a role in immune and inflammatory disease, such as rheumatoid arthritis and inflammatory bowel disease and potentially chronic obstructive pulmonary disease. These data were generated by analysis of 93870 expression in human cells and tissues and by comparison of the expression of 93870 in disease *versus* normal conditions. The *in vivo* arthritis data also show a progression of increasing 93870 expression which correlates with disease severity in an arthritis animal model. All of these diseases are disclosed in the specification at paragraphs [0055] and [0056]. The data disclosing 93870 expression in monocytes and macrophages, cells well-known to be involved in immune and inflammatory responses, also would lead the skilled practitioner to recognize the potential for 93870 to be involved in additional inflammatory diseases not elaborated on by Dr. Grant.

Dr. Grant's data, confirming a role for 93870 GPCR in immune and inflammatory diseases, including arthritis and inflammatory bowel disease and potentially chronic obstructive pulmonary disease, confirms for the skilled artisan that the specification discloses specific, well-established and credible utility. A skilled artisan would recognize that an alteration in expression and/or activity of 93870 GPCR plays a role in these diseases, and thus that a molecule recognizing 93870 protein of SEQ ID NO:2 or nucleic acids of SEQ ID NOs:1 or 3 could be useful in the diagnosis or prognosis of these diseases. The skilled artisan further would understand that modulating the expression of activity of 93870 GPCR can play a role in treating these diseases and thus would recognize the usefulness of screening assays to identify such molecules providing this effect. In view of these data and remarks, Applicant respectfully requests that this rejection be withdrawn.

Rejection of the Claims Under 35 U.S.C. §112, First Paragraph

Paragraph 7. Claims 28-29 and 32-43 are rejected under 35 U.S.C. §112, first paragraph on the grounds that, because the specification is not supported by either a specific and substantial asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. This rejection is respectfully traversed.

As evidenced by Dr. Ocain's declaration and supporting Exhibit B and the remarks above, one skilled in the art would know how to use the claimed invention to detect or modulate the expression or activity of 93870 nucleic acids or polypeptides in the cells and diseases disclosed in the specification and highlighted by Dr. Grant. Further, to supplement the skill in the art, for diagnostic methods and prognostic methods, the specification provides guidance, for example, at paragraphs [00246]-[00274]. The specification supplements the skill in the art for screening methods at, for example paragraphs [00183]-[00214]. Applicant notes that at the time of filing this application, one of skill in the art did not require a ligand to use an orphan GPCR, as evidenced by publications such as Wilson et al. (1998) attached as Exhibit C, the wide availability of known and surrogate ligands for GPCRs, well known assays for G protein signal transduction and well-known assays for activities disclosed in the specification at paragraphs [0050]-[0054]. This skill in the art, coupled with the teachings in the specification and expression results and relevant disease models provided by Dr. Grant's data, effectively teach one how to use the claimed invention. In view of these remarks, Applicant respectfully requests that this rejection be withdrawn.

CONCLUSIONS

The foregoing amendments and remarks are being made to place the Application in condition for allowance. Applicant respectfully requests reconsideration and the timely allowance of the pending claims because, in view of these amendments and remarks, Applicant respectfully submits that the rejections of claims 28-29 and 32-43 under 35 U.S.C. §§ 101 and 112 are herein overcome. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned.

This paper is being filed timely as a request for a three month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

27 March 2006

MILLENNIUM PHARMACEUTICALS, INC.

By _____

Tracy M. Sioussat, Ph.D.
Registration No. 50,609
40 Landsdowne Street
Cambridge, MA 02139
Telephone - 617-374-7679
Facsimile - 617-551-8820